CLAIMS

1. A method of regulating nicotine metabolism in an individual comprising selectively inhibiting CYP2A6.

2. The method defined in claim 1, wherein CYP2A6 is selectively inhibited using one or more of the following (i) substances which inhibit CYP2A6 activity; or (ii) substances which inhibit transcription and/or translation of the gene encoding CYP2A6.

3. The method defined in claim 1, wherein CYP2A6 is selectively inhibited by administering to the individual at least one compound having a lactone structure with a carbonyl moiety.

4. The method defined in claim 1, wherein CYP2A6 is selectively inhibited by administering to the individual at least one compound selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim-4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

5. The method defined in claim 4, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine, N-nitrosodimethylamine and mixtures thereof.

6. A method of screening for a substance that regulates nicotine metabolism to cotinine in an individual comprising assaying for a substance which (i) selectively

inhibits CYP2A6 activity, or (ii) selectively inhibits transcription and/or translation of the gene encoding CYP2A6.

7. A pharmaceutical composition for use in treating a condition requiring regulation of nicotine metabolism to cotinine comprising an effective amount of a substance which selectively inhibits CYP2A6, and a pharmaceutically acceptable carrier, diluent, or excipient.

8. The composition defined in claim 7, wherein the substance comprises at least one compound having a lactone structure with a carbonyl moiety.

9. The composition defined in claim 7, wherein the substance is at least one member selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim -4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

10. The composition defined in claim 9, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine, N-nitrosodimethylamine and mixtures thereof.

11. A method for treating a condition requiring regulation of nicotine metabolism to cotinine in an individual comprising administering to the subject an effective amount of a substance which selectively inhibits CYP2A6.

12. The method defined in claim 11, wherein the substance is at least one compound having a lactone structure with a carbonyl moiety.

13. The method defined in claim 11, wherein the substance is at least one member selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim 4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

14. The method defined in claim 13, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine, N-nitrosodimethylamine and mixtures thereof.

15. The method defined in any one of claims 12, comprising administration to the individual of a mixture comprising two or more of said substances.

16. The method defined in any one of claims 11-15, wherein the condition is dependent or non-dependent tobacco use.

17. A method for enhancing inhibition of nicotine metabolism by a CYP2A6 inhibitor in an individual comprising administering to the individual an effective amount of a substance which selectively inhibits CYP2A6, and an effective amount of an inhibitor of CYP2B6.

18. The method defined in claim 17, wherein the substance is at least one compound having a lactone structure with a carbonyl moiety.

19. The method defined in claim 17, wherein the substance is at least one member selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim

-4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

20. The method defined in claim 19, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine, N-nitrosodimethylamine and mixtures thereof.

21. A pharmaceutical composition for use in treating a condition requiring regulation of nicotine metabolism to cotinine comprising an effective amount of a substance which selectively inhibits CYP2A6, an effective amount of an inhibitor of CYP2B6, and/or a pharmaceutically acceptable carrier, diluent, or excipient.

22. The composition defined in claim 21, wherein the substance comprises at least one substance having a lactone structure with a carbonyl moiety.

23. The composition defined in claim 21, wherein the substance comprises at least one member selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim -4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

24. The composition defined in claim 23, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine, N-nitrosodimethylamine and mixtures thereof.

25. A method for treating a condition requiring regulation of nicotine metabolism to cotinine in an individual comprising administering to the individual an effective amount of a substance which selectively inhibits CYP2A6, and an effective amount of an inhibitor of CYP2B6.

26. The method defined in claim 25, wherein the substance is at least one compound having a lactone structure with a carbonyl moiety.

27. The method defined in claim 25, wherein the substance is at least one member selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim -4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

28. The method defined in claim 27, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine, N-nitrosodimethylamine and mixtures thereof.

29. The method defined in any one of claims 26-28, comprising administration to the individual of a mixture comprising two or more of said substance.

30. The method defined in any one of claims 25-29, wherein the condition is dependent or non-dependent tobacco use.

31. A method for determining the CYP2A6 activity in an individual containing two mutant alleles, one mutant allele or no mutant alleles at a gene locus for the CYP2A6 gene, the method comprising the steps of:

(a) assaying a DNA-containing bodily sample from the individual to determine whether the individual contains two mutant alleles, one mutant allele or no mutant alleles at the CYP2A6 gene locus;

(b) determining the amount of CYP2A6 present in the individual; and

(c) correlating the results of assaying in step (a) and the amount of CYP2A6 in step (b) to determine an appropriate dosage for that individual of a substance which (i) selectively inhibits CYP2A6 activity, or (ii) selectively inhibits transcription and/or translation of the gene encoding CYP2A6.

32. The method defined in claim 31, wherein the DNA-containing bodily sample is a blood sample.

33. The method defined in claim 31, wherein the DNA-containing bodily sample is a tissue sample.

34. Use of a substance which selectively inhibits CYP2A6 for the preparation of a medicant for regulation of nicotine metabolism to cotinine in an individual.

35. The use defined in claim 34, wherein the substance is at least one compound having a lactone structure with a carbonyl moiety.

36. The use defined in claim 34, wherein the substance is at least one member selected from the group consisting of coumarin, furanocoumarin, methoxsalen, imperatorin, psoralen, α-naphthoflavone, isopimpinellin, β-naphthoflavone, bergapten, sphondin, coumatetralyl (racumin), (+)-cis-3,5-dimethyl-2-(3-pyridyl)-thiazolidim -4-one, naringenin and related flavones, diethyldithiocarbamate, N-nitrosodialkylamine, nitropyrene, menadione, imidazole antimycotics, miconazole, clotrimazole, pilocarpine, hexamethylphosphoramide, 4-methylnitrosamine-3-pyridyl-1-butanol, aflatoxin B, analogs thereof and derivatives thereof.

37. The method defined in claim 36, wherein the N-nitrosodialkylamine is selected from the group consisting of N-nitrosodiethylamine. N-nitrosodimethylamine and mixtures thereof.

38. A method for treating a condition requiring regulation of nicotine metabolism to cotinine in an individual comprising administering to the subject: (a) an effective amount of a first substance which selectively inhibits CYP2A6; and (b) an effective amount of a second substance which is capable of regulating inhibition of the first substance.

add a12

add B1

add a13